Remarks/Argument

By the present amendment, claims 1 and 23 have been amended, and claim 37 has been added. Support for amended claims 1 and 23 can be found at at least p. 11, line 3 to p. 13, line 2 of the present application. Support for new claim 37 can be found at at least p. 6, ll. 28-31 of the present application.

Below is a discussion of the 35 U.S.C. §112, first paragraph, rejection of claims 1-2, 5, 7 and 21-23, and the 35 U.S.C. §102(b) rejection of claims 1-2, 5, 7, and 21-23.

1. 35 U.S.C. §112, first paragraph, rejection of claims 1-2, 5, 7, and 21-23.

Claims 1-2, 5, 7, and 21-23 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action argues the claims embrace an enormous number of vitronectin (VN) fragments constituting a claimed genus. Thus, the Office Action argues, the claims embrace a claimed genus that encompasses VN and/or fibronectin (FN) fragments yet to be discovered.

By the present amendment, claims 1 and 23 have been amended to recite "vitronectin (VN) or an integrin-receptor binding fragment thereof." Applicants respectively submit that this amendment to claims 1 and 23 should satisfy the requirements of 35 U.S.C. §112, first paragraph, because the present specification sufficiently describes the structure or functional nature of VN or an integrin-receptor binding fragment thereof. For example, the "Background of the Invention" section of the present application discusses the functional nature of VN (as reported in several scientific journal articles). Additionally, the specification discusses the

integrin-receptor binding function of VN at p. 11, line 3 to p. 13 of the present application.

Accordingly, Applicants respectively submit that amended claims 1 and 23 comply with the written description requirement, and request that the 35 U.S.C. §112, first paragraph, rejection of these claims be withdrawn. Additionally, Applicants respectively request that the 35 U.S.C. §112, first paragraph, rejection of claims 2, 5, 7 and 21-22, which depend directly from claim 1, be withdrawn.

2. 35 U.S.C. §102(b) rejection of claims 1-2, 5, 7, and 21-23.

Claims 1-2, 5, 7, and 21-23 were rejected under 35 U.S.C. §102(b) as being anticipated by PCT Pub. No. WO02/24219 to Upton *et al*. (hereinafter, "the '219 publication") as evidenced by Upton *et al*., *Comp. Biochem. Physiol*. (Part B) 121:35-41, 1998 (hereinafter, "Upton 1998"). The Office Action argues that the '219 publication teaches a mammalian cell culture system of human keratinocytes, wherein the medium is comprised of IGF-I and VN in the absence of serum. Additionally, the Office Action argues that Upton 1998 teaches binding assays of IGF-I to VN in the presence of IGFBP3 and in the absence of serum.

By the present amendment, claim 1 has been amended to more particularly point out and distinctly claim the present invention and to better define the present invention over the '219 publication and Upton 1998. More particularly, claim 1 has been amended to include the further features that: (1) the IGFBP is selected from the group consisting of IGFBP3 and IGFBP5; and (2) the cell culture medium comprises VN or an integrin-receptor binding fragment thereof.

Applicants respectively submit that amended claim 1 is not anticipated by the '219 publication and Upton 1998 because neither of these references discloses each and every feature recited in amended claim 1. As noted above, the Office Action relies on the '219 publication as teaching a mammalian cell culture system of human keratinocytes, wherein the medium comprises (i) IGF-1, (ii) VN, and (iii) an absence of serum. In doing so, the Office Action appears to have misconstrued the '219 publication because the medium disclosed in the '219 publication, unlike the medium recited in amended claim 1, is a serum-containing medium. For example, the Office Action relies on Example 4 of the '219 publication as teaching a medium suitable for cell culture. Example 4, however, does not teach a medium suitable for cell culture because all that Example 4 teaches is a buffering solution (*i.e.*, HEPES or TES) suitable for optimizing interactions between radio-labeled ligands and their cell surface receptors. The serum-containing medium described in Example 4 would not have been suitable for culturing cells, especially with regard to the specific culturing requirements of epithelial cells (*i.e.*, primary keratinocytes).

Also in support of the 35 U.S.C. §102(b) rejection, the Office Action relies upon Upton 1998, even though Example 4 of the '219 publication refers the reader to Upton *et al.*, *Endocrinology*, 140:2928-2931, 1999 (hereinafter, "Upton 1999"). Further, the Office Action cites the "*2.3.2 IGF Binding Studies*" section at p. 37, 2nd column of Upton 1998.

Applicants respectfully submit that that the binding assay medium disclosed by Upton 1998 was used purely as a buffering solution to optimize binding of radio-labeled ligands to cell-surface receptors and, hence, would not be suitable for

cell culture. In fact, the binding experiments described in Upton 1998 were undertaken using a method and a serum-containing HEPES-binding buffer previously disclosed by Ross *et al.*, *Biochem J.*, 258:267-272, 1989 (hereinafter, "Ross"). For example, in the section headed "*IGF Binding to Cell Receptors*" (p. 268, 1st column), Ross discloses a HEPES buffer comprising 0.5% Bovine Serum Albumin (emphasis added). Additionally, Applicants wish to emphasize the fact that HEPES is a zwitterion buffer that is suitable for modulating the pH of a medium and not for supporting cell growth. In contrast to the serum-free mammalian cell culture system recited in amended claim 1, which is suitable for cell culture, the medium disclosed by Ross and Upton 1998 is a serum-containing medium that would not be suitable for cell culture.

Concerning the Office Action's citation of Upton 1998 instead of Upton 1999, Applicants have addressed below the teachings of Upton 1999 (and the references cited therein) to avoid these citations at a time subsequent to the present amendment. The "*Binding Assays*" section described by Upton 1999 (p. 2929, 1st column) refers to a serum-containing HEPES- and TES-binding media previously used by Ballard *et al.*, *Biochem. J.*, 249:721-726, 1988 (hereinafter, "Ballard 1988"), and originally described by Ballard *et al.*, *Biochem. J.*, 233:223-230, 1986 (hereinafter, "Ballard 1986"). (See, *e.g.*, the "*IGF Binding Experiments*" section on p. 722, 1st column of Ballard 1988, and p. 224, 2nd column of Ballard 1986). The primary purpose of the HEPES- and TES-binding buffers described in Ballard 1986 and Ballard 1988 was to control the pH of the buffers (*i.e.*, reduce acidity) and optimize the binding of radio-labeled ligands to their cell surface receptors. In

contrast to the cell culture medium recited in amended claim 1, which recites a serum-free medium that is suitable for cell culture, Upton 1999 teaches a serum-containing medium that would not be suitable for cell culture and that is not designed to support cell growth.

Accordingly, Applicants respectfully submit that none of the references relied upon by the Office Action teach each and every feature of the mammalian cell culture recited in amended claim 1 (*i.e.*, a non-serum-containing medium), and request that the 35 U.S.C. §102(b) rejection of claim 1 be withdrawn. Additionally, Applicants respectively request that the 35 U.S.C. §102(b) rejection claims 2, 5, 7 and 21-23, which depend directly from amended claim 1, be withdrawn.

Please charge any deficiency or credit any overpayment in the fees for this matter to our Deposit Account No. 20-0090.

Respectfully submitted,

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